DOCKET NO.: NIHB-2264 PATENT

**Application No.:** 10/722,000

Office Action Dated: October 20, 2009

This listing of claims will replace all prior versions, and listings, of claims in the application.

## **Listing of Claims:**

1. (Currently Amended) An infectious chimeric respiratory syncytial virus (RSV) comprising a major nucleocapsid (N) protein, a nucleocapsid phosphoprotein (P), a large polymerase protein (L), a RSV M2 ORF1 RNA polymerase elongation factor (M2(ORF1)), and a partial or complete human RSV genome or antigenome of one RSV A strain or subgroup combined with a heterologous gene or gene segment of a bovine or mouse RSV strain or subgroup virus to form a chimeric RSV genome or antigenome, wherein the chimeric genome or antigenome is further modified by one or more attenuating mutations selected from the group consisting of Phe<sub>521</sub>, Gln<sub>831</sub>, Met<sub>1169</sub> and Tyr<sub>1321</sub> of the L-protein to another amino acid, or a nucleotide substitution of base T to C at position of 7605 in the gene-start sequence of gene M2 comprising genome segments encoding antigenic determinants of RSV B F and G glycoproteins, wherein the RSV A genome or antigenome contains the following attenuating mutations:

- i) a mutation encoding V267I in the N gene;
- ii) a mutation encoding C319Y in the L gene;
- iii) a mutation encoding H1690Y in the L gene;
- iv) a mutation encoding Q831L in the L gene;
- v) a mutation encoding D1183D in the L gene;
- vi) a point mutation T to C at nucleotide 7806 of the gene start of the M2 gene; and wherein the RSV A genome or antigenome further contains at least one of the following:

| a mutation encoding Y1321N in the L gene; or |
|--|
| a deletion of the SH open reading frame.     |

2 - 19. (Canceled)

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20. (Previously Presented) The chimeric RSV of claim 1, wherein the chimeric genome or antigenome includes at least one attenuating mutation stabilized by multiple

nucleotide changes in a codon specifying the mutation.

21. (Canceled)

22. (Original) The chimeric RSV of claim 1 further comprising a nucleotide

modification specifying a phenotypic change selected from a change in growth

characteristics, attenuation, temperature-sensitivity, cold-adaptation, plaque size, host-range

restriction, or a change in immunogenicity.

23. (Original) The chimeric RSV of claim 22, wherein a SH, NS1, NS2,

M2ORF2, or G gene is modified.

24. (Original) The chimeric RSV of claim 23, wherein the SH, NS1, NS2,

M2ORF2, or G gene is deleted in whole or in part or expression of the gene is ablated by

introduction of one or more stop codons in an open reading frame of the gene.

25. - 27. (Canceled)

28. (Original) The chimeric RSV of claim 22, wherein the nucleotide

modification comprises an insertion, deletion, substitution, or rearrangement of a translational

start site within the chimeric genome or antigenome.

29. – 34. (Canceled)

35. (Original) The chimeric RSV of claim 1 which is a virus.

36. (Original) The chimeric RSV of claim 1 which is a subviral particle.

37. - 45. (Canceled)

46. (Original) An immunogenic composition to elicit an immune response against

RSV comprising an immunologically sufficient amount of the chimeric RSV of claim 1 in a

physiologically acceptable carrier.

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47. (Original) The immunogenic composition of claim 46, formulated in a dose of  $10^3$  to  $10^6$  PFU.

48. (Original) The immunogenic composition of claim 46, formulated for administration to the upper respiratory tract by spray, droplet or aerosol.

49. – 65. (Canceled)